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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,970	08/10/2001	Ashok Amin	AMIN4A	4363

7590 02/25/2002

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EXAMINER
WORTMAN, DONNA C

ART UNIT	PAPER NUMBER
1648	5

DATE MAILED: 02/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/925,970	Applicant(s) AMIN ET AL.	
	Examiner Donna C. Wortman, Ph.D.	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The use of the trademarks ENBREL and REMICADE has been noted in this application. Each should be fully capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3 and 5 are indefinite because it is not clear what is encompassed by "a compound that neutralizes the effect of secreted TNF alpha." The specific examples of such a compound given are etanercept, which is a recombinant TNF p75 receptor, and infliximab, a humanized monoclonal antibody that binds TNF alpha. It is not clear whether "a compound that neutralizes the effect of secreted TNF alpha" is intended to be limited to compounds that actually bind to TNF alpha and prevent its interaction with cell surface receptors, or whether the cited phrase would also encompass any compound that interferes with or prevents any and all effects of secreted TNF alpha. For example, would a compound that interferes with the activity of GM-CSF be encompassed? Would various anti-inflammatory and/or immunomodulatory drugs that do not actually bind TNF alpha be encompassed?

Claims 3 and 4 are indefinite in reciting "p75:FC inhibitor" which terminology is confusing since it is not clear whether "p75:FC inhibitor" is a type of inhibitor, or is that which is to be inhibited.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method for treating any type of hepatitis (claims 1 and 3-5) or a method for treating various types of viral hepatitis (claim 2) by administering a compound that neutralizes the effect of secreted TNF alpha (claims 1 and 2) which may be either "a p75:FC inhibitor" (claims 3 and 4) or a humanized monoclonal antibody (claims 5 and 6). The specification teaches the administration of etanercept to a single patient with rheumatoid arthritis and hepatitis C, after which the patient showed an improvement in arthritis symptoms, transaminase levels and viral RNA levels. It is apparent that one of skill in the art would not be able to extrapolate from the results from administering a single compound, etanercept, to a single patient with rheumatoid arthritis and hepatitis C, to obtain a method of treating any type of hepatitis, viral or nonviral, by administering any compound that can be interpreted as neutralizing the effect of secreted TNF alpha as is claimed. Even if the claims were to be limited to

treating hepatitis C by administration of etanercept, the specification would not teach one of skill in the art how to practice the invention as claimed, since a result observed in a single patient is not seen to enable a treatment method. The state of the art is properly considered in evaluating enablement. Campbell et al. (European Journal of Gastroenterology and Hepatology 13(2):191-192, 2001), cited on PTO 892, attached, (not prior art) disclose treatment of a patient with Crohn's disease, who also had chronic hepatitis C, with infliximab. Campbell et al. report no change in the raised level of the liver enzyme alanine aminotransferase and, despite the fact that the PCR for HCV was reported to be negative at 16 weeks follow-up, Campbell et al. do not suggest that infliximab is a treatment for hepatitis C, but rather interpret this result observed in a single patient differently: "... it would appear that in this particular case infliximab therapy was not detrimental to ongoing HCV infection" (page 192). Campbell provides evidence that a single case report does not provide those of skill in the art with sufficient teaching to practice a method of treatment, since the lack of a bad result in a single case cannot be extrapolated to a reasonable expectation for success in obtaining a generally beneficial result as is required in order to enable a treatment method.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by The Merck Manual of Diagnosis and Therapy (Beers et al., Eds., Seventeenth Edition,

published by Merck Research Laboratories, 1999) pages 384-386, cited on PTO 892, attached. The Merck Manual discloses treatment of autoimmune hepatitis with corticosteroids and treatment of hepatitis B and hepatitis C with interferon alpha, and discloses that both treatments result in reduction of inflammation. Because the scope of the claims is unclear insofar as the meaning of "a compound that neutralizes the effect of secreted TNF alpha," as discussed above, the hepatitis treatments disclosed by the Merck Manual are deemed to anticipate the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is 703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:30-5:00 and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Donna C. Wortman, Ph.D.
Primary Examiner
Art Unit 1648

dcw
February 21, 2002